

## PARENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 21 January 1999 (21.01.99)	
<b>International application No.</b> PCT/GB98/01683	<b>Applicant's or agent's file reference</b> N68867B GCW
<b>International filing date</b> (day/month/year) 09 June 1998 (09.06.98)	<b>Priority date</b> (day/month/year) 09 June 1997 (09.06.97)
<b>Applicant</b> BALDWIN, Thomas, John et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
04 January 1999 (04.01.99)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer Lazar Joseph Panakal</p> <p>Telephone No.: (41-22) 338.83.38</p>
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From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

WOODS, Geoffrey Corlett  
J.A. KEMP & CO.  
14 South Square  
Gray's Inn  
London WC1R 5LX  
GRANDE BRETAGNE

Action:  
**PCT**

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year)

03.09.99

Applicant's or agent's file reference  
N.68867B GCW

IMPORTANT NOTIFICATION

International application No.  
PCT/GB98/01683

International filing date (day/month/year)  
09/06/1998

Priority date (day/month/year)  
09/06/1997

Applicant

MEDICAL RESEARCH COUNCIL et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 apmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Peralt Lappas, R

Tel. +49 89 2399-8052





## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference N.68867B GCW		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB98/01683	International filing date (day/month/year) 09/06/1998	Priority date (day/month/year) 09/06/1997	
International Patent Classification (IPC) or national classification and IPC C12N15/00			
Applicant MEDICAL RESEARCH COUNCIL et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 3 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input checked="" type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 04/01/1999		Date of completion of this report 03.09.99	
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80299 Munich Tel. +49 89 2399 - 0 Tx: 523656 apmu d Fax: +49 89 2399 - 4465		Authorized officer BULCAO DE MELO ..., T  Telephone No. +49 89 2399 8972	

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB98/01683

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-3,5-33	as originally filed		
4	as received on	11/08/1999 with letter of	11/08/1999

**Claims, No.:**

2-6,8-22,24	as originally filed		
1,7,23	as received on	11/08/1999 with letter of	11/08/1999

**Drawings, sheets:**

1/11-11/11	as originally filed
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**2. The amendments have resulted in the cancellation of:**

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**4. Additional observations, if necessary:**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB98/01683

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or Industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)	Yes:	Claims	1-24
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-24
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-20 and 22-24
	No:	Claims	21 (No Assessment, see section V, item 5)

**2. Citations and explanations**

see separate sheet

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

see separate sheet

## INTERNATIONAL PRELIMINARY

International application No. PCT/GB98/01683

EXAMINATION REPORT - SEPARATE SHEET

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## SECTION I

1. The amended claims 1, 7 and 23 filed with your letter of 11.08.99 are considered to be allowable under Article 34 (2) (b) PCT.

## SECTION V

2. Reference is made to the following documents:

D1: WO-A-94 05326

3. Novelty (Article 33(2) PCT)

The subject-matter of the present application does not appear to be disclosed in the prior art as defined in the regulations (Rule 64 (1)-(3) PCT).

Therefore, in view of such prior art the subject-matter of the present application (claims 1-24) has to be regarded as being new (Article 33 (2) PCT).

4. Inventive Step (Article 33 (3) PCT)

The closest prior art to evaluate the inventiveness of the present application (claims 1-24) is document D1.

Document D1 discloses a live vaccine strain of pathogenic bacteria, such as *E. coli*, comprising at least one mutation selected from a pyrimidine pathway mutation, such as in the *pyrB* gene, and an iron metabolism mutation, such as in the *fur* gene, said mutation providing attenuation of the virulence of said bacteria.

(See Abstract, page 7, line 15-page 16, line 3 and claims).

It is known in the prior art that one difficulty with the production of live attenuated vaccines is that during bulk culture the organism does not always express some proteins which are important for host protection. In addition, once such vaccines have been administered to the host, the vaccine strain does not have the optimum time or metabolic resources during its limited colonisation to express these proteins *in vivo* to a sufficient level to confer protection.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**International application No. PCT/GB98/01683

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The claimed attenuated bacteria strain differs from the one of D1 in that the native *fur* gene is modified such that its expression is regulated independently of the iron concentration in the environment of the bacteria.

Starting from D1, the underlying **technical problem** to be solved by the present application (**claims 1-24**) can be considered to lie in the provision of an alternative attenuated bacteria which produces said proteins which are important for host protection and are normally not produced in attenuated strains.

The **solution** provided by the Applicant to solve the above problem is an attenuated bacteria in which the native *fur* gene is modified such that the expression of the *fur* gene product is regulated independently of the iron concentration in the environment of the bacteria.

Neither D1 nor any of the cited prior art documents discloses nor suggests that altering the regulation of the ferric uptake regulation (*fur*) gene, such that its expression is independent of the iron concentration in the environment of the bacteria, enhances the expression of important protective antigens when the bacteria is grown in culture.

Therefore, there is no indication in the prior art that would teach the person skilled in the art to modify the native *fur* gene of attenuated bacteria, such that its expression is regulated independently of the iron concentration in the environment of the bacteria.

The attenuated bacteria of the present invention, which is the solution provided by the Applicant to solve the above problem, has thus the advantage of having increased expression of said protective antigens. Consequently live vaccines comprising said attenuated bacteria have increased efficacy when administered.

Thus, in view of the above, an inventive step can be acknowledged for the subject-matter of the present application (**claims 1-24**).

**INTERNATIONAL PRELIMINARY**

International application No. PCT/GB98/01683

**EXAMINATION REPORT - SEPARATE SHEET**

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**5. Industrial Applicability (Article 33(4) PCT)**

- 5.1. The subject-matter of present **claims 1-20 and 22-24** is susceptible of industrial applicability as defined in **Article 33(4) PCT**.
- 5.2. For the assessment of the present **claim 21** on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**SECTION VII**

6. Contrary to the requirements of **Rule 5.1(a)(ii) PCT**, the relevant background art disclosed in document **D1** is not mentioned in the description, nor is this document identified therein.





PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>C12N 15/00, A61K 39/095, C12R 1/36</b>	<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 98/56901</b> <b>(43) International Publication Date:</b> 17 December 1998 (17.12.98)
<b>(21) International Application Number:</b> PCT/GB98/01683 <b>(22) International Filing Date:</b> 9 June 1998 (09.06.98)  <b>(30) Priority Data:</b> 9711964.8                      9 June 1997 (09.06.97)                      GB  <b>(71) Applicant (for all designated States except US):</b> MEDICAL RESEARCH COUNCIL [GB/GB]; 20 Park Crescent, London W1N 4AL (GB).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> BALDWIN, Thomas, John [GB/GB]; Institute of Infections & Immunity, University Hospital, Nottingham NG7 2UH (GB). BORRIELLO, Saverio, Peter [GB/GB]; Public Health Laboratory Service, Central Public Health Laboratory, 61 Colindale Avenue, London NW9 5HT (GB). PALMER, Helen, Mary [GB/GB]; Public Health Laboratory Service, Bristol Royal Infirmary, Marlborough Street, Bristol BS2 8HW (GB).  <b>(74) Agent:</b> WOODS, Geoffrey, Corlett; J.A. Kemp & Co., 14 South Square, Gray's Inn, London WC1R 5LX (GB).		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>  <b>(88) Date of publication of the international search report:</b> 18 March 1999 (18.03.99)
<b>(54) Title:</b> LIVE ATTENUATED VACCINES  <b>(57) Abstract</b>  An attenuated bacterium in which the native <i>fur</i> gene, or homologue thereof, is modified such that the expression of the <i>fur</i> gene product, or homologue thereof, is regulated independently of the iron concentration in the environment of the bacterium, is suitable for use as a live vaccine. The bacterium may be, in particular, <i>Neisseria meningitidis</i> .		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01683

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 6 C12N15/00 A61K39/095 C12R1/36

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N A61K C12R

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 05326 A (UNIV SASKATCHEWAN) 17 March 1994 see abstract see page 7, line 15 - page 8, line 18 see page 11, line 4 - line 8 see page 12, line 6 - line 13 see page 12, line 20 - line 22 see claims ---	1-3, 5-7, 19-24
A	WO 87 02678 A (OREGON STATE) 7 May 1987 see abstract see page 1, line 1 - page 2, line 17 see page 3, line 6 - line 27 ---	1-5, 19
A	EP 0 322 237 A (WELLCOME FOUND) 28 June 1989 see abstract ---	3, 5, 6, 15, 16
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

18 December 1998

Date of mailing of the international search report

12/01/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
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 Fax: (+31-70) 340-3016

Authorized officer

Panzica, G

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 98/01683

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PINTOR M. ET AL.: "Blocking of iron uptake from transferrin by antibodies against the transferrin binding proteins in <i>Neisseria meningitidis</i>"</p> <p>MICROBIAL PATHOGENESIS, vol. 20, no. 3, 1996, pages 127-139, XP002085216 see abstract</p>	<p>1-5, 15, 16, 19-21</p>

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 98/01683

**Box I Observation where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 20, 21  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim(s) 20 and 21  
is(are) directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 98/01683

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9405326 A	17-03-1994	AT 173166 T	15-11-1998
		AU 683221 B	06-11-1997
		AU 4939193 A	29-03-1994
		DE 69322092 D	17-12-1998
		EP 0659086 A	28-06-1995
		IL 106903 A	10-01-1997
		US 5747309 A	05-05-1998
WO 8702678 A	07-05-1987	US 4681761 A	21-07-1987
		AU 594400 B	08-03-1990
		AU 6623286 A	19-05-1987
		EP 0245433 A	19-11-1987
		JP 63502427 T	14-09-1988
EP 0322237 A	28-06-1989	AU 2919389 A	19-07-1989
		CA 1327331 A	01-03-1994
		DE 3888652 D	28-04-1994
		DE 3888652 T	07-07-1994
		DK 412689 A	22-08-1989
		ES 2061700 T	16-12-1994
		WO 8905856 A	29-06-1989
		IE 65176 B	04-10-1995
		IL 88766 A	31-07-1995
		JP 2602970 B	23-04-1997
		JP 2502785 T	06-09-1990
		KR 9710759 B	30-06-1997
		US 5811105 A	22-09-1998
		US 5770214 A	23-06-1998

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>N68867B GCW</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 98/ 01683</b>	International filing date (day/month/year) <b>09/06/1998</b>	(Earliest) Priority Date (day/month/year) <b>09/06/1997</b>
Applicant <b>MEDICAL RESEARCH COUNCIL et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ **Certain claims were found unsearchable** (see Box I).
2. ☐ **Unity of invention is lacking** (see Box II).
3. ☒ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
  - ☐ filed with the international application.
  - ☒ furnished by the applicant separately from the international application,
    - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
  - ☐ Transcribed by this Authority
4. With regard to the **title**, ☒ the text is approved as submitted by the applicant
  - ☐ the text has been established by this Authority to read as follows:
5. With regard to the **abstract**, ☒ the text is approved as submitted by the applicant
  - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the **drawings** to be published with the abstract is:
  - Figure No.            ☐ as suggested by the applicant.
  - ☐ because the applicant failed to suggest a figure.
  - ☐ because this figure better characterizes the invention.
  - ☒ None of the figures.

# INTERNATIONAL SEARCH REPORT

ational application No.

PCT/GB 98/ 01683

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 20, 21  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claim(s) 20 and 21  
is(are) directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 98/01683

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/00 A61K39/095 C12R1/36

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N A61K C12R

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 05326 A (UNIV SASKATCHEWAN) 17 March 1994 see abstract see page 7, line 15 - page 8, line 18 see page 11, line 4 - line 8 see page 12, line 6 - line 13 see page 12, line 20 - line 22 see claims ---	1-3, 5-7, 19-24
A	WO 87 02678 A (OREGON STATE) 7 May 1987 see abstract see page 1, line 1 - page 2, line 17 see page 3, line 6 - line 27 ---	1-5, 19
A	EP 0 322 237 A (WELLCOME FOUND) 28 June 1989 see abstract ---	3, 5, 6, 15, 16

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Date of the actual completion of the international search

18 December 1998

Date of mailing of the international search report

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/AB 98/01683

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PINTOR M. ET AL.: "Blocking of iron uptake from transferrin by antibodies against the transferrin binding proteins in <i>Neisseria meningitidis</i>."</p> <p>MICROBIAL PATHOGENESIS, vol. 20, no. 3, 1996, pages 127-139, XP002085216 see abstract</p> <p>-----</p>	<p>1-5,15, 16,19-21</p>

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 98/01683

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9405326	A	17-03-1994	AT 173166 T	15-11-1998
			AU 683221 B	06-11-1997
			AU 4939193 A	29-03-1994
			DE 69322092 D	17-12-1998
			EP 0659086 A	28-06-1995
			IL 106903 A	10-01-1997
			US 5747309 A	05-05-1998
WO 8702678	A	07-05-1987	US 4681761 A	21-07-1987
			AU 594400 B	08-03-1990
			AU 6623286 A	19-05-1987
			EP 0245433 A	19-11-1987
			JP 63502427 T	14-09-1988
EP 0322237	A	28-06-1989	AU 2919389 A	19-07-1989
			CA 1327331 A	01-03-1994
			DE 3888652 D	28-04-1994
			DE 3888652 T	07-07-1994
			DK 412689 A	22-08-1989
			ES 2061700 T	16-12-1994
			WO 8905856 A	29-06-1989
			IE 65176 B	04-10-1995
			IL 88766 A	31-07-1995
			JP 2602970 B	23-04-1997
			JP 2502785 T	06-09-1990
			KR 9710759 B	30-06-1997
			US 5811105 A	22-09-1998
			US 5770214 A	23-06-1998